<u>REMARKS</u>

This application is a continuation of U.S. Serial No. 08/24,843 which has now issued as U.S. Patent No. 6,274,148. Accordingly, the specification has been amended to update the status of the related applications. Additionally, the Title has been amended to more clearly reflect the subject matter now being claimed.

Claim 20 has been amended to recite the invention with greater particularity. In this regard, claim 20 now recites that the glycoprotein of the assay kit has "mannose-terminated glycosylation" and that "less than about 10% of the total N-linked carbohydrate on said HCV glycoprotein is sialic acid." Support for this recitation may be found at, e.g., page 5, lines 10-12. Additionally, the claim now recites that the "HCV glycoprotein is selected from the group consisting of a glycoprotein expressed from the E1 region of HCV, a glycoprotein expressed from the E2 region of HCV, and aggregates thereof." Support for this recitation is found in claims 1 and 2 as originally filed, as well as throughout the specification, at page 5, line 14 through page 6, line 3.

New claims 44-79 have been added. New claims 44-68 pertain to antibodies specific for HCV glycoproteins having mannose-terminated glycosylation, wherein less than about 10% of the total N-linked carbohydrate on said HCV glycoprotein is sialic acid. New claims 69-79 recite embodiments analogous to those recited in new claims 44-79 but are directed to assay kits and ultimately depend from claim 20.

Support for the new claims is as specified above, as well as in claim 20 as originally filed and throughout the specification at, e.g., page 6, lines 22-23; page 10, lines 8-12; and page 15, lines 2-4.

Entry of the foregoing amendments is respectfully requested.

Please direct all further communications in this application to:

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Respectfully submitted,

Date: 9/27/01

By: 🥆

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<u>VERSION WITH MARKINGS TO SHOW CHANGES MADE</u>

In the Title:

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The title has been amended as follows:

ANTIBODIES TO HEPATITIS C VIRUS ASIALOGLYCOPROTEINS

In the Specification:

The paragraph on page 1, lines 13-16 has been amended as follows:

This application is a continuation of U.S. Serial No. 08/249,843, filed May 26, 1994, now U.S. Patent No. 6,274,148, which in turn is a continuation-in-part of [copending] U.S. Serial No. 07/758,880, filed September 13, 1991, now abandoned, which is a continuation-in-part of U.S. Serial No. 07/611,419, filed November 8, 1990, now abandoned, the disclosures of which are incorporated herein by reference.

In the Claims:

Claim 20 has been amended as follows:

20. (Amended) An assay kit for detecting the presence of <u>a</u> hepatitis C virus (HCV) [asialoglycoproteins] <u>glycoprotein having mannose-terminated glycosylation</u>, wherein less than about 10% of the total N-linked carbohydrate on said HCV glycoprotein is sialic acid, wherein said HCV glycoprotein is selected from the group consisting of a glycoprotein expressed from the E1 region of HCV, a glycoprotein expressed from the E2 region of HCV, and aggregates thereof, said kit comprising:

a solid support;

a mannose-binding protein; and an <u>isolated</u> antibody specific for said HCV [asialoglycoprotein] <u>glycoprotein</u>;

wherein one of said antibody and said mannose binding protein is bound to said solid support.

Claims 1-19 and 24-43 have been canceled, and the following new claims have been added:

- 44. (New) An isolated antibody specific for a hepatitis C virus (HCV) glycoprotein having mannose-terminated glycosylation, wherein less than about 10% of the total N-linked carbohydrate on said HCV glycoprotein is sialic acid, wherein said HCV glycoprotein is selected from the group consisting of a glycoprotein expressed from the E1 region of HCV, a glycoprotein expressed from the E2 region of HCV, and aggregates thereof.
- 45. (New) The antibody of claim 44, wherein said HCV glycoprotein is a glycoprotein expressed from the E1 region of HCV.
- 46. (New) The antibody of claim 44, wherein said HCV glycoprotein is a glycoprotein expressed from the E2 region of HCV.
- 47. (New) The antibody of claim 44, wherein said HCV glycoprotein is an aggregate of a glycoprotein expressed from the E1 region of HCV and a glycoprotein expressed from the E2 region of HCV.
- 48. (New) The antibody of claim 44, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E1 region of HCV.
- 49. (New) The antibody of claim 44, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E2 region of HCV.

50. (New) The antibody of claim 44, wherein the antibody is a polyclonal antibody.

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- 51. (New) The antibody of claim 45, wherein the antibody is a polyclonal antibody.
- 52. (New) The antibody of claim 46, wherein the antibody is a polyclonal antibody.
- 53. (New) The antibody of claim 47, wherein the antibody is a polyclonal antibody.
- 54. (New) The antibody of claim 48, wherein the antibody is a polyclonal antibody.
- 55. (New) The antibody of claim 49, wherein the antibody is a polyclonal antibody.
- 56. (New) An isolated antibody specific for a hepatitis C virus (HCV) glycoprotein having mannose-terminated glycosylation, wherein less than about 10% of the total N-linked carbohydrate on said HCV glycoprotein is sialic acid, wherein said HCV glycoprotein is selected from the group consisting of a glycoprotein expressed from the E1 region of HCV, a glycoprotein expressed from the E2 region of HCV, and aggregates thereof, and further wherein said HCV glycoprotein is produced by the method comprising the steps of:

growing a host cell transformed with a structural gene encoding an HCV glycoprotein expressed from the E1 region of HCV or the E2 region of HCV in a suitable culture medium;

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causing expression of said structural gene, under conditions inhibiting sialylation; and

isolating said HCV glycoprotein from said cell culture by contacting said HCV glycoprotein with a mannose-binding protein specific for mannose-terminated glycoproteins, and isolating the protein that binds to said mannose-binding protein.

- 57. (New) The antibody of claim 56, wherein said HCV glycoprotein is a glycoprotein expressed from the E1 region of HCV.
- 58. (New) The antibody of claim 56, wherein said HCV glycoprotein is a glycoprotein expressed from the E2 region of HCV.
- 59. (New) The antibody of claim 56, wherein said HCV glycoprotein is an aggregate of a glycoprotein expressed from the E1 region of HCV and a glycoprotein expressed from the E2 region of HCV.
- 60. (New) The antibody of claim 56, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E1 region of HCV.
- 61. (New) The antibody of claim 56, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E2 region of HCV.
- 62. (New) The antibody of claim 56, wherein the antibody is a polyclonal antibody.

63. (New) The antibody of claim 57, wherein the antibody is a polyclonal antibody.

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- 64. (New) The antibody of claim 58, wherein the antibody is a polyclonal antibody.
- 65. (New) The antibody of claim 59, wherein the antibody is a polyclonal antibody.
- 66. (New) The antibody of claim 60, wherein the antibody is a polyclonal antibody.
- 67. (New) The antibody of claim 61, wherein the antibody is a polyclonal antibody.
- 68. (New) The antibody of claim 56, wherein the structural gene is linked to a sequence encoding a secretion leader that directs the glycoprotein to the endoplasmic reticulum and said conditions inhibiting sialylation comprise inhibiting transport of glycoproteins from the endoplasmic reticulum to the golgi.
- 69. (New) The assay kit of claim 20, wherein said HCV glycoprotein is a glycoprotein expressed from the E1 region of HCV.
- 70. (New) The assay kit of claim 20, wherein said HCV glycoprotein is a glycoprotein expressed from the E2 region of HCV.

71. (New) The assay kit of claim 20, wherein said HCV glycoprotein is an aggregate of a glycoprotein expressed from the E1 region of HCV and a glycoprotein expressed from the E2 region of HCV.

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- 72. (New) The assay kit of claim 20, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E1 region of HCV.
- 73. (New) The assay kit of claim 20, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E2 region of HCV.
- 74. (New) The assay kit of claim 20, wherein the antibody is a polyclonal antibody.
- 75. (New) The assay kit of claim 69, wherein the antibody is a polyclonal antibody.
- 76. (New) The assay kit of claim 70, wherein the antibody is a polyclonal antibody.
- 77. (New) The assay kit of claim 71, wherein the antibody is a polyclonal antibody.
- 78. (New) The assay kit of claim 72, wherein the antibody is a polyclonal antibody.
- 79. (New) The assay kit of claim 73, wherein the antibody is a polyclonal antibody.--

CURRENTLY PENDING CLAIMS

20. (Amended) An assay kit for detecting the presence of <u>a</u> hepatitis C virus (HCV) glycoprotein having mannose-terminated glycosylation, wherein less than about 10% of the total N-linked carbohydrate on said HCV glycoprotein is sialic acid, wherein said HCV glycoprotein is selected from the group consisting of a glycoprotein expressed from the E1 region of HCV, a glycoprotein expressed from the E2 region of HCV, and aggregates thereof, said kit comprising:

a solid support;

a mannose-binding protein; and an isolated antibody specific for said HCV glycoprotein;

wherein one of said antibody and said mannose binding protein is bound to said solid support.

- 44. (New) An isolated antibody specific for a hepatitis C virus (HCV) glycoprotein having mannose-terminated glycosylation, wherein less than about 10% of the total N-linked carbohydrate on said HCV glycoprotein is sialic acid, wherein said HCV glycoprotein is selected from the group consisting of a glycoprotein expressed from the E1 region of HCV, a glycoprotein expressed from the E2 region of HCV, and aggregates thereof.
- 45. (New) The antibody of claim 44, wherein said HCV glycoprotein is a glycoprotein expressed from the E1 region of HCV.
- 46. (New) The antibody of claim 44, wherein said HCV glycoprotein is a glycoprotein expressed from the E2 region of HCV.

47. (New) The antibody of claim 44, wherein said HCV glycoprotein is an aggregate of a glycoprotein expressed from the E1 region of HCV and a glycoprotein expressed from the E2 region of HCV.

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- 48. (New) The antibody of claim 44, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E1 region of HCV.
- 49. (New) The antibody of claim 44, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E2 region of HCV.
- 50. (New) The antibody of claim 44, wherein the antibody is a polyclonal antibody.
- 51. (New) The antibody of claim 45, wherein the antibody is a polyclonal antibody.
- 52. (New) The antibody of claim 46, wherein the antibody is a polyclonal antibody.
- 53. (New) The antibody of claim 47, wherein the antibody is a polyclonal antibody.
- 54. (New) The antibody of claim 48, wherein the antibody is a polyclonal antibody.
- 55. (New) The antibody of claim 49, wherein the antibody is a polyclonal antibody.

56. (New) An isolated antibody specific for a hepatitis C virus (HCV) glycoprotein having mannose-terminated glycosylation, wherein less than about 10% of the total N-linked carbohydrate on said HCV glycoprotein is sialic acid, wherein said HCV glycoprotein is selected from the group consisting of a glycoprotein expressed from the E1 region of HCV, a glycoprotein expressed from the E2 region of HCV, and aggregates thereof, and further wherein said HCV glycoprotein is produced by the method comprising the steps of:

growing a host cell transformed with a structural gene encoding an HCV glycoprotein expressed from the E1 region of HCV or the E2 region of HCV in a suitable culture medium;

causing expression of said structural gene, under conditions inhibiting sialylation; and

isolating said HCV glycoprotein from said cell culture by contacting said HCV glycoprotein with a mannose-binding protein specific for mannose-terminated glycoproteins, and isolating the protein that binds to said mannose-binding protein.

- 57. (New) The antibody of claim 56, wherein said HCV glycoprotein is a glycoprotein expressed from the E1 region of HCV.
- 58. (New) The antibody of claim 56, wherein said HCV glycoprotein is a glycoprotein expressed from the E2 region of HCV.
- 59. (New) The antibody of claim 56, wherein said HCV glycoprotein is an aggregate of a glycoprotein expressed from the E1 region of HCV and a glycoprotein expressed from the E2 region of HCV.

- 60. (New) The antibody of claim 56, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E1 region of HCV.
- 61. (New) The antibody of claim 56, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E2 region of HCV.
- 62. (New) The antibody of claim 56, wherein the antibody is a polyclonal antibody.
- 63. (New) The antibody of claim 57, wherein the antibody is a polyclonal antibody.
- 64. (New) The antibody of claim 58, wherein the antibody is a polyclonal antibody.
- 65. (New) The antibody of claim 59, wherein the antibody is a polyclonal antibody.
- 66. (New) The antibody of claim 60, wherein the antibody is a polyclonal antibody.
- 67. (New) The antibody of claim 61, wherein the antibody is a polyclonal antibody.
- 68. (New) The antibody of claim 56, wherein the structural gene is linked to a sequence encoding a secretion leader that directs the glycoprotein to the endoplasmic

reticulum and said conditions inhibiting sialylation comprise inhibiting transport of glycoproteins from the endoplasmic reticulum to the golgi.

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- 69. (New) The assay kit of claim 20, wherein said HCV glycoprotein is a glycoprotein expressed from the E1 region of HCV.
- 70. (New) The assay kit of claim 20, wherein said HCV glycoprotein is a glycoprotein expressed from the E2 region of HCV.
- 71. (New) The assay kit of claim 20, wherein said HCV glycoprotein is an aggregate of a glycoprotein expressed from the E1 region of HCV and a glycoprotein expressed from the E2 region of HCV.
- 72. (New) The assay kit of claim 20, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E1 region of HCV.
- 73. (New) The assay kit of claim 20, wherein said HCV glycoprotein is an aggregate of glycoproteins expressed from the E2 region of HCV.
- 74. (New) The assay kit of claim 20, wherein the antibody is a polyclonal antibody.
- 75. (New) The assay kit of claim 69, wherein the antibody is a polyclonal antibody.
- 76. (New) The assay kit of claim 70, wherein the antibody is a polyclonal antibody.

- 77. (New) The assay kit of claim 71, wherein the antibody is a polyclonal antibody.
- 78. (New) The assay kit of claim 72, wherein the antibody is a polyclonal antibody.
- 79. (New) The assay kit of claim 73, wherein the antibody is a polyclonal antibody.